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# OBSERVATIONS ON CAPACITY FACTOR DETERMINATION FOR REVERSED-PHASE LIQUID CHROMATOGRAPHY WITH AQUEOUS METHANOL ELUENTS USING THE SOLUBILITY PARAMETER CONCEPT MODEL AND ITS DERIVATIVES

T. L. HAFKENSCHEID and E. TOMLINSON*

*Physical Pharmacy Group, Department of Pharmacy, University of Amsterdam, Plantage Muidergracht 24, 1018 TV Amsterdam (The Netherlands)*

SUMMARY

By recasting the solubility parameter concept model of solute chromatographic behaviour in reversed-phase systems, it is shown that use of the Hildebrand solubility parameter term leads to an inherent overestimation of the retention parameter, $k'$, by a factor of approximately 4.5. This is similar also to that found using the solubility parameter term for determining the aqueous solubility of liquid solutes. Further, for reversed-phase ODS systems using aqueous methanol eluents, a semi-empirical relationship, based on derivatives of the solubility parameter concept model, has been derived to calculate capacity factors at one eluent composition from those obtained at another. Additionally, it is shown how liquid–liquid distribution coefficients may be used with this semi-empirical relationship to calculate capacity factors directly.

INTRODUCTION

Prediction of solute retention and phase selectivity is an aspect of modern liquid chromatography which is gaining increasing attention. For reversed-phase systems, approaches to this may be grouped into those based on physical (or phenomenological) models, and those founded using semi-empirical (or analogous) descriptions of solute behaviour. Included as examples of the former are the solubility parameter concept model[1,2] and the solvophobicity theory approach[3,4]; as an example of the latter type are the studies of Tanaka *et al.*[5] and of Colin and Guiochon[6].

Although the solubility parameter concept model has been favourably received conceptually, its weakness is regarded[2] as being due to its limitation in only qualitatively describing chromatographic behaviour. In this contribution we attempt to recast the solubility parameter concept model (and its derivatives), in order to examine its ability to determine quantitatively solute chromatographic behaviour.

EXPERIMENTAL

The solutes studied (Table I) were obtained from various sources and were generally of analytical or synthetic grade purity. N,N-Dimethylaminododecane was obtained from Fluka (Buchs, Switzerland) and was of 95% purity. The stationary phase material was Hypersil ODS (5 μm) from Ahrin (Rijswijk, The Netherlands). Eluents were made up volumetrically from combinations of analytical-reagent grade methanol (Baker, Deventer, The Netherlands) and (depending on the type of solute chromatographed) (i) doubly-distilled water (I), (ii) ammonium phosphate buffer (pH 2.15) containing 80 mmol $l^{-1}$ $NH_4^+$ (II), (iii) ammonium phosphate buffer (pH 7.00) containing 80 mmol $l^{-1}$ $NH_4^+$ (III) or (iv) ammonium phosphate buffer (pH 7.00) containing 80 mmol $l^{-1}$ $NH_4^+$ and 0.8 mmol $l^{-1}$ N,N-dimethylaminododecane (IV).

High-performance liquid chromatographic (HPLC) equipment and columns (50 × 4.6 mm) and procedures were as described previously[7].

RESULTS AND DISCUSSION

From regular solution theory[8], the non-ideality of liquid–liquid interactions in binary systems is given by

$$\ln \gamma_i = \frac{\bar{V}_i \varphi_j^2}{RT} (\delta_i - \delta_j)^2 \tag{1}$$

where the Hildebrand solubility parameter, $\delta$, which is defined as the square root of a compounds cohesive energy density, is a measure of intermolecular forces in the liquid state. Assuming that, for sparingly soluble liquids, $\varphi_j^2 \approx 1$, eqn. 1 becomes

$$\ln \gamma_i = \frac{\bar{V}_i}{RT} (\delta_i - \delta_j)^2 \tag{2}$$

implying that the solute's activity coefficient is independent of concentration. Tijssen et al.[2] and Schoenmakers et al.[9,10] have adapted eqn. 2 to describe the interactions of a solute with both stationary and mobile phases in reversed-phase chromatography. By assuming that the stationary phase in such a system behaves as a liquid, these workers have given the capacity factor of a solute as

$$\log k_i' = \frac{\bar{V}_i}{2.3RT} [(\delta_i - \delta_m)^2 - (\delta_i - \delta_s)^2] + \log (n_s/n_m) \tag{3}$$

Eqn. 3 cannot be directly used to calculate retention because both $\delta_s$ and $n_s$ are, for bonded phases, difficult to assess. However, if we assume that the effects of the mobile phase (and variations in its composition) on the stationary phase are negligible, then we may assume that $\delta_s$ and $n_s$ are constants. From this, eqn. 3 may be used to calculate the alteration in solute capacity factor for any one system with a change in the mobile phase composition of that system; that is, by using

$$\Delta \log k_i' = \frac{\bar{V}_i}{2.3RT} [(\delta_i - \delta_{m_1})^2 - (\delta_i - \delta_{m_2})^2] + \log (n_{m_2}/n_{m_1}) \tag{4}$$

where subscripts 1 and 2 refer to two mobile phases of different composition. Assuming zero compressibility of the mobile phase with the chromatographic column, then the ratio of the mobile phase contents of any one column may be expressed as

$$\frac{n_{m_2}}{n_{m_1}} = \frac{\left(\sum_j \frac{\varphi_j}{\bar{V}_j}\right)_{m_2}}{\left(\sum_j \frac{\varphi_j}{\bar{V}_j}\right)_{m_1}} \tag{5}$$

Further, as $\delta_m$ for a mobile phase composed of two or more solvents may be found from the solubility parameters of the pure solvents using

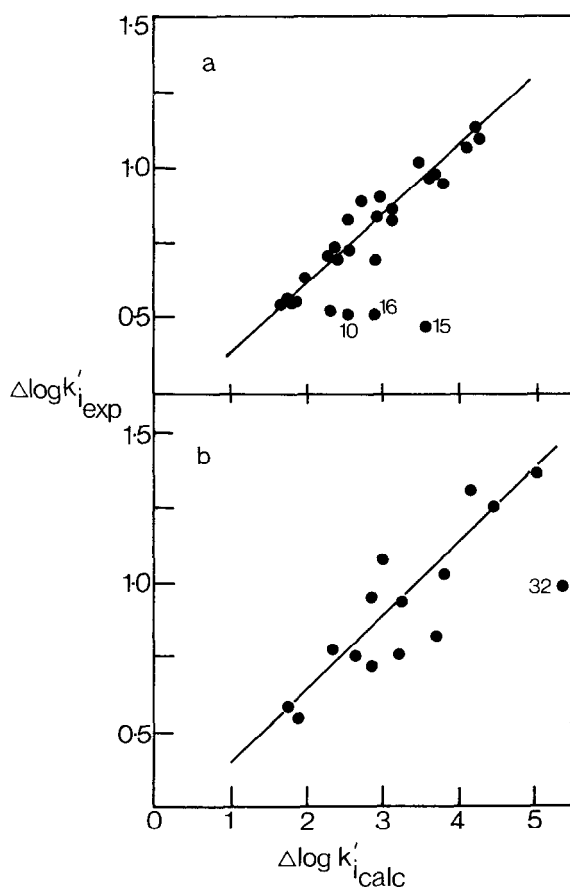$$\delta_m = \sum_j \varphi_j \delta_j \tag{6}$$



Fig. 1. Relationships between $\Delta\log k'_{i,\text{exp}}$ and $\Delta\log k'_{i,\text{calc}}$ (eqn. 7), using values from (a) this study and (b) from ref. 14. Numbers next to outlier points refer to the compounds in Table I. The line in (a) is the regression line according to eqn. 10 and that in (b) is the regression line according to eqn. 11.

TABLE I

PHYSICOCHEMICAL PARAMETERS AND EXPERIMENTALLY OBSERVED AND CALCULATED $\Delta LOG\ k'_i$ VALUES (EQN. 7) FOR SOME LIQUID SOLUTES

| No. | Solute | $\delta_i$ $(cal^{1/2}\cdot ml^{-3/2})$ | $\bar{V}_i$ at 20°C $(ml\cdot mol^{-1})$ | This study* | | Schoenmakers et al.[14]** | |
|---|---|---|---|---|---|---|---|
| | | | | $\Delta Log\ k'_{i,exp}$ | $\Delta Log\ k'_{i,calc}$ | $\Delta Log\ k'_{i,exp}$ | $\Delta Log\ k'_{i,calc}$ |
| 1 | Water | 23.53 | 18.05 | 0.000*** | -0.434 | | |
| 2 | Methanol | 14.50 | 40.54 | | | | |
| 3 | Dichloromethane | 9.88 | 64.02 | 0.549 | 1.631 | | |
| 4 | Trichloromethane | 9.16 | 80.49 | 0.715 | 2.270 | | |
| 5 | Tetrachloromethane | 8.55 | 96.50 | 0.899 | 2.937 | | |
| 6 | Butan-1-ol | 11.60 | 91.53 | 0.546 | 1.843 | | |
| 7 | Pentan-1-ol | 11.12 | 108.24 | 0.694 | 2.371 | | |
| 8 | Hexan-1-ol | 10.77 | 125.59 | 0.857 | 2.913 | | |
| 9 | Cyclohexane | 8.19 | 108.10 | 1.031 | 3.432 | | |
| 10 | Cyclohexanone | 10.42 | 103.56 | 0.508 | 2.508 | | |
| 11 | 2-Chloropropane | 8.07 | 91.15 | 0.688 | 2.916 | | |
| 12 | 2-Nitropropane | 9.97 | 90.21 | 0.521 | 2.309 | | |
| 13 | 2-Methylpropanoic acid | 11.96 | 91.60 | 0.560 | 1.733 | | |
| 14 | Hexanoic acid | 11.68 | 125.25 | 0.828 | 2.522 | | |
| 15 | Diethyl ether | 7.53 | 103.84 | 0.465 | 3.524 | | |
| 16 | Ethyl acetate | 8.91 | 97.88 | 0.505 | 2.862 | | |
| 17 | Benzene | 9.16 | 88.91 | 0.725 | 2.517 | 0.751 | 2.605 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 18 | Toluene | 8.93 | 106.30 | 0.847 | 3.109 | 0.929 | 3.238 |
| 19 | Chlorobenzene | 9.67 | 101.79 | 0.897 | 2.720 | 0.947 | 2.791 |
| 20 | Nitrobenzene | 10.86 | 102.28 | 0.730 | 2.324 | 0.772 | 2.313 |
| 21 | Aniline | 11.73 | 91.15 | 0.554 | 1.795 | 0.584 | 1.727 |
| 22 | Ethylbenzene | 8.84 | 122.46 | 0.968 | 3.633 | 1.031 | 3.794 |
| 23 | Benzyl alcohol | 12.05 | 103.80 | 0.633 | 1.945 | 0.539 | 1.850 |
| 24 | Methyl benzoate | 10.19 | 125.06 | 0.821 | 3.144 | 0.748 | 3.195 |
| 25 | Ethyl benzoate | 9.75 | 143.47 | 0.948 | 3.833 | | |
| 26 | Propylbenzene | 8.64 | 139.44 | 1.118 | 4.243 | 1.241 | 4.450 |
| 27 | Isopropylbenzene | 8.60 | 139.48 | 1.090 | 4.263 | | |
| 28 | Butylbenzene | 8.58 | 156.05 | | | 1.363 | 5.033 |
| 29 | $p$-Xylene | 8.83 | 123.30 | 0.971 | 3.663 | | |
| 30 | $o$-Dichlorobenzene | 10.04 | 112.67 | | | 1.083 | 2.934 |
| 31 | Dimethyl phthalate | 11.01 | 163.12 | | | 0.819 | 3.664 |
| 32 | Diethyl phthalate | 9.97 | 198.87 | | | 0.977 | 5.331 |
| 33 | Acetophenone | 10.58 | 116.88 | | | 0.722 | 2.793 |
| 34 | Diphenyl ether | 10.10 | 158.36 | | | 1.300 | 4.136 |
| 35 | Mesitylene | 8.88 | 138.93 | 1.076 | 4.115 | | |

$\star$ Using $\varphi_{m_1} = 0.50$ and $\varphi_{m_2} = 0.75$; $n_{m_2}/n_{m_1} = 0.808$.

$\star\star$ Using $\varphi_{m_1} = 0.60$ and $\varphi_{m_2} = 0.90$; $n_{m_2}/n_{m_1} = 0.751$.

$\star\star\star$ By definition (water being the unretained solute).

it follows that eqn. 4 may be recast as

$$\Delta\log k'_i = \frac{\overline{V}_i}{2.3RT} \{ [\delta_i - (\sum_j \varphi_j\delta_j)_{m_1}]^2 - [\delta_i - \sum_j \varphi_j\delta_j)_{m_2}]^2 \} +$$

$$\log\left(\sum_j \frac{\varphi_j}{\overline{V}_j}\right)_{m_2} - \log\left(\sum_j \frac{\varphi_j}{\overline{V}_j}\right)_{m_1} \tag{7}$$

It is apparent that eqn. 7 may be used to examine whether the solubility parameter-based retention model can estimate changes in retention with changes in mobile phase composition.

Thus, for solutes that are liquids at 20°C, we have calculated $\Delta\log k'_i$ values for methanol–water systems using eqn. 7 with $\overline{V}_i$, $\overline{V}_j$ and $\delta_i$, $\delta_j$ values from the literature[11–13] (Table I). Calculated values have been compared with experimental values obtained in the present study using Hypersil octadecylsilane with $\varphi_{m_1} = 0.50$ and $\varphi_{m_2} = 0.75$ ($n_{m_2}/n_{m_1} = 0.808$), as well as values calculated from the work of Schoenmakers et al.[14] who reported $k'_i$ values for a number of liquids using Nucleosil octadecylsilane as stationary phase, and with $\varphi_{m_1}$ as 0.60 and $\varphi_{m_2}$ as 0.90 ($n_{m_2}/n_{m_1} = 0.751$). Calculated and experimental values are given in Table I. Comparison of these shows large differences, with calculated values being overestimated by a factor of 4–5. Fig. 1a and b illustrates the concordance between both sets of calculated and observed $\Delta\log k'_i$ values. As given by eqns. 8 and 9, there exist only reasonable agreement between these sets of values, viz.,

(i)  present study:

$$\Delta\log k'_{i,\text{exp}} = 0.21(0.03)\, \Delta\log k'_{i,\text{calc}} + 0.16(0.07) \tag{8}$$
$$(n = 28;\, r = 0.855;\, F = 90.4)$$

(ii)  for data from ref. 14:

$$\Delta\log k'_{i,\text{exp}} = 0.18(0.04)\, \Delta\log k'_{i,\text{calc}} + 0.31(0.14) \tag{9}$$
$$(n = 15;\, r = 0.790;\, F = 21.7)$$

(where $n$, $r$ and $F$ are the number of data values, the linear regression correlation coefficient with its standard deviation in parentheses and the variance ratio value, respectively). For both comparisons, the relations are strongly perturbed by, for eqn. 8, compounds 10, 15 and 16 (Table 1), and for eqn. 9, compound 32. Omitting these outliers leads to, respectively

$$\Delta\log k'_{i,\text{exp}} = 0.23(0.01)\, \Delta\log k'_{i,\text{calc}} + 0.15(0.04) \tag{10}$$
$$(n = 25;\, r = 0.963;\, F = 292).$$

and

$$\Delta\log k'_{i,\text{exp}} = 0.24(0.04)\, \Delta\log k'_{i,\text{calc}} + 0.15(0.12) \tag{11}$$
$$(n = 14;\, r = 0.887;\, F = 44.3)$$

A remarkable feature of these two equations is that there are no significant differences between their slope coefficients and their intercept coefficients, indicating that, although significant outliers exist, both equations could have some validity for calculating changes in (liquid) solute retention with alterations in eluent composition.

To examine whether the overestimation of $\Delta\log k_i'$ found using eqn. 7 is inherent in the use of Hildebrand's solubility parameter *per se*, we have used $\delta$ to calculate directly a further physico-chemical parameter of liquid solutes, *viz.*, their aqueous solubility. For these solvents eqn. 2 holds (*i.e.*, $\varphi_j^2 \approx 1$), such that $\log \gamma_i$ becomes independent of solute concentration. Thus:

$$\log \gamma_{i,_w} = \log \gamma_{i,_w}^{\text{sat}} = -\log X_{i,_w} = \frac{\bar{V}_i}{2.3RT} (\delta_i - \delta_j)^2 \tag{12}$$

Table II gives $-\log X_{i,_w}$ values calculated using eqn. 12 for 59 liquids, for which experimentally determined aqueous solubilities also exist[15,16]. Direct comparison between calculated and observed solubilities (Fig. 2) reveals that considerable deviations exist, with both an overestimation in predicted value being obtained using eqn. 12 and no clear correlation between the two values. Some structure between the two can be identified however. First, by omitting diethyl ether and the three studied aliphatic amines from the data set we find, using linear regression, that
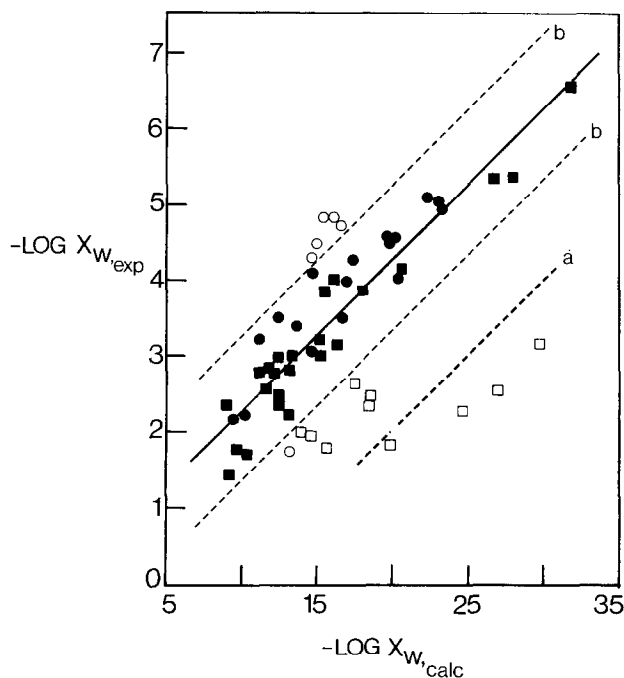


Fig. 2. Relationship between observed aqueous solubilities of liquids and those calculated using eqn. 12. Compounds outside the dashed line (a) are diethyl ether and some aliphatic amines; only compounds between lines (b) have been included in the regression analysis (eqn. 14). Circles and squares indicate aromatic and aliphatic solutes, respectively.

TABLE II

PHYSICO-CHEMICAL PARAMETERS AND OBSERVED AND CALCULATED (EQN. 12) AQUEOUS SOL-
UBILITIES (AT 20°C) FOR SOME LIQUID SOLUTES

| No. | Solute | $\delta_i$ $(cal^{1/2} \cdot ml^{-3/2})$ | $\bar{V}_i$ $(ml \cdot mol^{-1})$ | $- Log\ X_{w,exp}$ | $- Log\ X_{w,calc}$ |
|---|---|---|---|---|---|
| 1 | Dichloromethane | 9.88 | 64.02 | 2.37 | 8.89 |
| 2 | Trichloromethane | 9.16 | 80.49 | 2.98 | 12.39 |
| 3 | Tetrachloromethane | 8.55 | 96.50 | 4.02 | 16.14 |
| 4 | Chloroethane | 8.55 | 71.86 | 2.78 | 12.02 |
| 5 | 1,1-Dichloroethane | 8.92 | 84.17 | 3.01 | 13.40 |
| 6 | 1,2-Dichloroethane | 9.86 | 80.12 | 2.79 | 11.16 |
| 7 | 1,1,1-Trichloroethane | 9.16 | 99.63 | 3.86 | 15.34 |
| 8 | Bromoethane | 8.91 | 74.62 | 2.81 | 11.89 |
| 9 | 1-Chloropropane | 8.39 | 88.16 | 3.20 | 15.07 |
| 10 | 2-Chloropropane | 8.07 | 91.15 | 3.14 | 16.24 |
| 11 | 1-Nitropropane | 10.29 | 88.37 | 2.54 | 11.55 |
| 12 | 2-Nitropropane | 9.97 | 90.21 | 2.46 | 12.36 |
| 13 | 2-Methylpropanoic acid | 11.96 | 91.60 | 1.44 | 9.14 |
| 14 | Vinyl ethyl ether | 7.82 | 95.03 | 2.64 | 17.49 |
| 15 | Diethyl ether | 7.53 | 103.84 | 1.84 | 19.82 |
| 16 | Ethyl acetate | 8.91 | 97.88 | 1.78 | 15.60 |
| 17 | 1-Chlorobutane | 8.37 | 104.46 | 3.86 | 17.90 |
| 18 | Butan-1-ol | 11.60 | 91.53 | 1.75 | 9.71 |
| 19 | Isobutanol | 11.24 | 92.86 | 1.69 | 10.46 |
| 20 | Ethyl propionate | 8.77 | 114.53 | 2.46 | 18.60 |
| 21 | Pentan-1-ol | 11.12 | 108.24 | 2.35 | 12.43 |
| 22 | Pentan-3-ol | 10.16 | 107.34 | 1.97 | 14.31 |
| 23 | 2-Methylbutan-1-ol | 10.76 | 107.59 | 2.22 | 13.08 |
| 24 | 3-Methylbutan-2-ol | 10.02 | 107.17 | 1.95 | 14.59 |
| 25 | Hexanoic acid | 11.68 | 125.25 | 2.81 | 13.11 |
| 26 | 2,2-Dimethylbutane | 6.71 | 132.89 | 5.35 | 28.03 |
| 27 | 2,3-Dimethylbutane | 6.97 | 130.26 | 5.36 | 26.64 |
| 28 | Hexan-1-ol | 10.77 | 125.59 | 2.99 | 15.24 |
| 29 | 3,3-Dimethyl-1-butan-2-ol | 9.51 | 125.81 | 2.39 | 18.44 |
| 30 | Dipropylamine | 7.97 | 136.74 | 2.28 | 24.69 |
| 31 | Triethylamine | 7.42 | 139.09 | 2.57 | 26.92 |
| 32 | Octan-1-ol | 10.30 | 157.47 | 4.13 | 20.55 |
| 33 | Dibutylamine | 8.15 | 168.51 | 3.18 | 29.72 |
| 34 | Dodecan-1-ol | 9.78 | 224.24 | 6.54 | 31.61 |
| 35 | Thiophene | 9.84 | 79.01 | 3.19 | 11.04 |
| 36 | Cyclohexane | 8.19 | 108.10 | 4.81 | 16.24 |
| 37 | Cyclohexanone | 10.42 | 103.56 | 1.75· | 13.27 |
| 38 | Benzene | 9.16 | 88.91 | 3.38 | 13.69 |
| 39 | Toluene | 8.93 | 106.30 | 3.98 | 16.89 |
| 40 | Fluorobenzene | 9.11 | 94.00 | 3.53 | 14.57 |
| 41 | Chlorobenzene | 9.67 | 101.79 | 4.09 | 14.58 |
| 42 | Bromobenzene | 9.87 | 105.03 | 4.28 | 14.61 |
| 43 | Iodobenzene | 10.13 | 111.43 | 4.52 | 14.92 |
| 44 | Nitrobenzene | 10.86 | 102.28 | 3.51 | 12.24 |
| 45 | Aniline | 11.73 | 91.15 | 2.17 | 9.46 |
| 46 | Benzyl alcohol | 12.05 | 103.80 | 2.19 | 10.20 |
| 47 | Methyl benzoate | 10.19 | 125.06 | 3.48 | 16.59 |
| 48 | Ethyl benzoate | 9.75 | 143.47 | 4.04 | 20.31 |
| 49 | Ethylbenzene | 8.84 | 122.46 | 4.55 | 19.70 |

TABLE II (*continued*)

| No. | Solute | $\delta_i$ $(cal^{1/2} \cdot ml^{-3/2})$ | $\bar{V}_i$ $(ml \cdot mol^{-1})$ | $-Log\ X_{w,exp}$ | $-Log\ X_{w,calc}$ |
|-----|--------|------|------|------|------|
| 50 | Propylbenzene | 8.64 | 139.44 | 5.05 | 23.05 |
| 51 | Isopropylbenzene | 8.60 | 139.48 | 4.94 | 23.18 |
| 52 | o-Xylene | 9.06 | 120.62 | 4.50 | 18.83 |
| 53 | m-Xylene | 8.88 | 122.83 | 4.56 | 19.66 |
| 54 | p-Xylene | 8.83 | 123.30 | 4.51 | 19.86 |
| 55 | o-Dichlorobenzene | 10.04 | 112.67 | 4.87 | 15.29 |
| 56 | m-Dichlorobenzene | 9.80 | 114.10 | 4.82 | 16.04 |
| 57 | Styrene | 9.35 | 114.97 | 4.28 | 17.24 |
| 58 | Acetophenone | 10.58 | 116.88 | 3.05 | 14.62 |
| 59 | Mesitylene | 8.88 | 138.93 | 5.13 | 22.23 |

$$-\log X_{w,exp} = -0.20(0.02) \log X_{w,calc} + 0.34(0.35) \tag{13}$$
$$(n = 55;\ r = 0.790;\ F = 85.7)$$

and, after omission of a second set of outliers, consisting mainly of aliphatic esters, branched alcohols and halobenzenes, then we find (Fig. 2)

$$-\log X_{w,exp} = -0.20(0.01) \log X_{w,calc} + 0.33(0.20) \tag{14}$$
$$(n = 43;\ r = 0.936;\ F = 290)$$

Comparison of eqns. 8–11 with eqn. 14 indicates that the magnitudes of the deviations between experimental solute parameters and those calculated using Hildebrand's solubility parameter are very similar, regardless of the parameters studied, and that its use introduces an error in parameter overestimation by a factor of between 4.2 and 5.0 [although for use of the solubility parameter concept in prediction of retention it is obvious that the assumption that the effects of the mobile phase (and variations in its composition) on the stationary phase are negligible, is totally valid, we consider it highly improbable that this can lead to such a large parameter overestimation].

The solubility parameter concept model of solute retention in reversed-phase systems (*i.e.*, eqn. 3) may be reconstructed[10] so as to relate solute capacity factor to the volume fraction of organic modifier present in a binary eluent, *viz.*,

$$\log k'_i = A\varphi_m^2 + B\varphi_m + C \tag{15}$$

where the constant $C$ represents the (hypothetical) logarithmic capacity factor using purely aqueous eluents, *i.e.*, $\log k'_{w,i}$. It has been postulated by Snyder *et al.*[17] that for most practical situations the quadratic term in eqn. 15 be omitted, such that

$$\log k'_i = \log k'_{w,i} - S\varphi_m \tag{16}$$

where the constant $S$ is regarded[17] as being dependent only on the type of eluent organic modifier used. However, experimentally it has been found that $S$ is not

TABLE III

DERIVED REGRESSION FOR THE RELATIONSHIP $S = p \log k'_{i,w} + q$

Values in parentheses are standard deviations.

| Reference | Stationary phase | Regression coefficients and statistics for the relationship $S = p \log k'_{w_i} + q$ | | | | | |
|---|---|---|---|---|---|---|---|
| | | $p$ | $q$ | $n$ | $r$ | $F$ | Eqn. |
| Hafkenscheid and Tomlinson[7] | Hypersil ODS | 0.74(0.04) | 1.62(0.09) | 32* | 0.960 | 349 | 19 |
| Hafkenscheid and Tomlinson[16] | Hypersil ODS | 0.79(0.02) | 1.57(0.06) | 104** | 0.959 | 1283 | 20 |
| Schoenmakers et al.[14] | Nucleosil 10RP-18 | 0.69(0.04) | 1.54(0.09) | 49** | 0.944 | 384 | 21 |
| Schoenmakers et al.[14] | Nucleosil 10RP-18 | 0.75(0.06) | 1.29(0.14) | 30** | 0.930 | 180 | 22 |
| Hammers et al.[18] | Lichrosorb RP-18 | 0.73(0.02) | 1.52(0.06) | 76* | 0.981 | 1887 | 23 |
| Mean*** | | 0.74(0.03) | 1.56(0.04) | | | | |

\* $S$ and $\log k'_{w,i}$ values taken directly from the original papers.

\*\* $S$ and $\log k'_{w,i}$ values calculated from $\log k'_i$ values reported at two or more values of $\varphi_m$ using eqn. 16.

\*\*\* Omitting outlier $q$ value from eqn. 22.

invariant with solute, and that some linear relationships between $S$ and $\log k'_{w,i}$ exist, i.e.,

$$S = p \log k'_{w,i} + q \tag{17}$$

These relationships have been reported by Schoenmakers et al.[10], by ourselves[7] and by Hammers et al.[18] for methanol–water eluents, which reinforces the comment[10] that $S$ is dependent on both the phase system and the solute(s) under study.

If the coefficients of eqn. 17 could be obtained with some certainty, then it should be possible to use a derivative of eqn. 16 to calculate solute retention at various eluent compositions. Thus first, by introducing eqn. 17 into eqn. 16, we obtain

$$\log k'_i = (1 - p\varphi_m) \log k'_{w,i} - q\varphi_m \tag{18}$$

Although for tetrahydrofuran–water and acetonitrile–water eluents little correlation between $S$ and $\log k'_{w,i}$ can be shown[10], for methanol–water eluents this is possible, and Table III gives the relevant relationships derived between $S$ and $\log k'_{w,i}$, with values for $p$ and $q$ (eqn. 18) being given (eqns. 19–23). Thus, using empirically found values for $p$ and $q$ (Table III), we may now write

$$\log k'_i = (1 - 0.74\ \varphi_m) \log k'_{w,i} - 1.56\ \varphi_m \tag{24}$$

Owing to its origin, eqn. 24 should be generally applicable to reversed-phase systems consisting of an ODS-type stationary phase and a binary aqueous methanol eluent. Eqn. 24 appears to be useful for the calculation of $\log k'$ at low $\varphi_m$ values from $\log k'$ values at higher $\varphi_m$ values. However, at high $\varphi_m$ values there is a problem of possible "cross-overs" occurring in $\log k'$ *versus* $\varphi_m$ plots[19–21], which cannot be accounted for by this equation.

Aware of this restriction, we have tested eqn. 24 using literature data for $\log k'$ at different $\varphi_m$ values. For example, McDuffie[19] has reported $\log k'$ values for various organic pollutants using a Zorbax-ODS column and aqueous methanol mobile phases, with $\varphi_m = 0.85$ and 0.75. Using $\log k'$ ($\varphi = 0.85$) to calculate $\log k'$ ($\varphi = 0.75$) values we find estimates that are between 59.7% and 90.7% of those experimentally found (with an average for $n = 15$ of 74.2%). Further, using the data of Wells et al.[20], calculations of $\log k'$ ($\varphi_m = 0.30$) from $\log k'$ ($\varphi_m = 0.50$) values gives estimates that are between 58.8%, (for barbitone) and 99.7%, (for methyl-*sec*.-pentylbarbitone) of the found values, with (for $n = 24$) a mean value of 85.4%, when using Partisil ODS as the stationary phase; with Partisil ODS-2 as the stationary phase estimates of $\log k'$ ($\varphi_m = 0.30$) are between 66.1% (amobarbitone) and 97.8% (barbitone) of the found values, with an average (for $n = 19$) of 77.0%. These findings indicate that eqn. 24 may be used to give reasonable estimates of $\log k'$ at one aqueous methanol eluent composition from another.

Although $\log k'_{w,i}$ values are not readily obtainable, the scope of eqn. 24 may be expanded by first recalling a number of studies[7,18,22] that have shown $\log k'_{w,i}$ to be very similar in value to the liquid–liquid distribution coefficients of solutes determined using octan-1-ol–water as the solvent pair. To examine this possibility, we have

TABLE IV

LITERATURE EXPERIMENTALLY DETERMINED OCTAN-1-OL–WATER DISTRIBUTION COEFFICIENTS AND THOSE CALCULATED FROM THE REPORTED ISOCRATIC $k_i$ VALUES USING EQN. 24

| No.* | McDuffie[19]** | | Wells et al.[20]*** | | | Braumann and Grimme[22]§ | | |
|---|---|---|---|---|---|---|---|---|
| | $Log\ K^{oct}_{d,exp}$ | $Log\ K^{oct}_{d,calc}$ ($\varphi_m = 0.75$) | $Log\ K^{oct}_{d,exp}$ | $Log\ K^{oct}_{d,calc}$ $\varphi_m = 0.30$ | $\varphi_m = 0.50$ | $Log\ K^{oct}_{d,exp}$ | $Log\ K^{oct}_{d,calc}$ $\varphi_m = 0.55$ | $\varphi_m = 0.60$ |
| 1 | 2.16 | 2.20 | 0.65 | 1.03 | 1.35 | 2.67 | 2.78 | 2.68 |
| 2 | 2.71 | 2.49 | 0.85 | 1.17 | 1.40 | 2.39 | 2.44 | 2.34 |
| 3 | 2.11 | 2.67 | 0.95 | 1.31 | 1.52 | 2.30 | 2.42 | 2.30 |
| 4 | 3.35 | 3.37 | 1.05 | 1.31 | 1.50 | 2.41 | 2.13 | 2.01 |
| 5 | 3.36 | 3.48 | 1.15 | 1.45 | 1.59 | 1.55 | 1.74 | 1.67 |
| 6 | 4.09 | 3.91 | 1.42 | 1.44 | 1.52 | 1.42 | 1.50 | 1.42 |
| 7 | 4.07 | 4.02 | 1.35 | 1.48 | 1.64 | 1.19 | 1.26 | 1.16 |
| 8 | 4.57 | 4.36 | 1.69 | 1.58 | 1.60 | 1.14 | 0.89 | 0.74 |
| 9 | 5.08 | 4.40 | 1.65 | 1.59 | 1.65 | | | |
| 10 | 4.54 | 4.47 | 1.45 | 1.62 | 1.69 | | | |
| 11 | 5.28 | 4.72 | 1.69 | 1.63 | 1.71 | | | |
| 12 | 5.18 | 4.85 | 1.65 | 1.68 | 1.72 | | | |
| 13 | 5.57 | 5.28 | 1.89 | 1.69 | 1.76 | | | |
| 14 | 5.90 | 5.66 | 1.57 | 1.75 | 1.74 | | | |
| 15 | 6.34 | 5.96 | 1.65 | 1.70 | 1.78 | | | |
| 16 | 1.58 | 1.96 | 1.65 | 1.78 | 1.84 | | | |
| 17 | 3.18 | 3.03 | 1.85 | 1.85 | 1.80 | | | |
| 18 | 2.99 | 3.28 | 2.07 | 1.96 | 1.95 | | | |

| | | | | | |
|---|---|---|---|---|---|
| 19 | 2.73 | 3.10 | 2.07 | 1.99 | 1.97 |
| 20 | 2.84 | 3.06 | 2.07 | 1.99 | 1.97 |
| 21 | 1.97 | 2.16 | 2.15 | 2.14 | 2.09 |
| 22 | 3.38 | 3.55 | 2.15 | 2.16 | 2.04 |
| 23 | 3.38 | 3.66 | 2.85 | 2.37 | 2.25 |
| 24 | 3.39 | 3.55 | 3.00 | 2.20 | 2.14 |
| 25 | 1.61 | 2.00 | | | |
| 26 | −0.42 | 0.25 | | | |
| 27 | 5.04 | 4.54 | | | |
| 28 | 0.98 | 1.69 | | | |
| 29 | 6.22 | 6.04 | | | |
| 30 | 5.04 | 4.92 | | | |
| 31 | 3.72 | 3.66 | | | |
| 32 | 1.85 | 2.13 | | | |
| 33 | 2.84 | 3.44 | | | |
| 34 | 4.67 | 4.67 | | | |
| 35 | 2.69 | 3.12 | | | |
| 36 | 4.18 | 4.11 | | | |
| 37 | 2.42 | 3.03 | | | |

* Compounds coded as in original publications.
** For organic pollutants, using a Zorbax ODS column.
*** For barbiturates, using a Partisil ODS column.
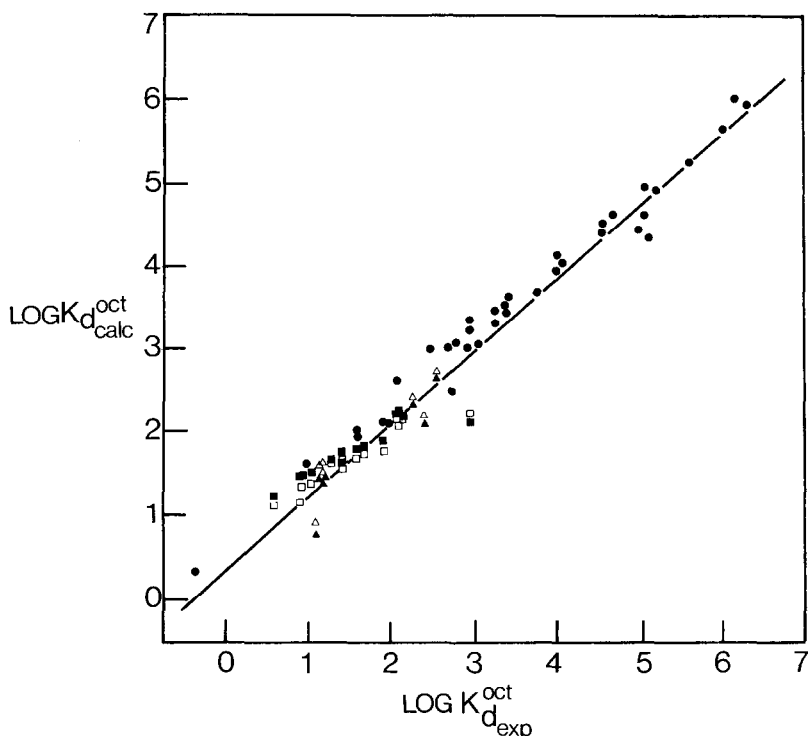§ For pyridazinones, using a LiChrosorb RP-18 column.

Fig. 3. Relationship between experimentally determined octan-1-ol–water solute distribution coefficients (log $K_{d,exp}^{oct}$) and those calculated from single isocratic chromatographic capacity factors using eqn. 24 (log $K_{d,calc}^{oct}$). Circles are for values calculated using $k'$ values with $\varphi_m = 0.75$[19]; open and closed squares are for values calculated using $\varphi_m = 0.50$ and $\varphi_m = 0.30$[20], respectively; open and closed triangles are for values calculated using $\varphi_m = 0.60$ and $\varphi_m = 0.55$[22], respectively. Overlapping data points (see Table IV) have been omitted for clarity. The line is the regression line according to eqn. 25.

taken log $k'_{w,i}$ to be analogous to log $K_d^{oct}$ (solute octan-1-ol–water distribution coefficient), and have calculated this latter value using eqn. 24 (where log $k'_{w,i}$ has been replaced by log $K_d^{oct}$) for solutes whose measured log $K_d^{oct}$ values and log $k'$ (isocratic) have been reported. Table IV gives these measured log $K_d^{oct}$ values and those calculated in this manner. As can be seen from Fig. 3, it is demonstrated that eqn. 24 can be used to adequately predict log $K_d^{oct}$ for solutes from single log $k'$ values determined at $\varphi_m$ compositions between 0.30 and 0.75, with the relationship between experimental and calculated values being given by

$$\log K_{d,calc}^{oct} = 0.88(0.02) \log K_{d,exp}^{oct} + 0.33(0.05) \qquad (25)$$
$$(n = 100; \; r = 0.976; \; F = 1977)$$

The statistics of this correlation and the previous discussion indicate that experimental log $K_d^{oct}$ values may be used with eqn. 24 to give reasonable estimates of log $k_i$ at $\varphi_m$ values between 0.30 and 0.75. (The converse, that log $k'_i$ values may be used to calculate log $K_d^{oct}$ values using eqn. 24 is of further interest to us[7,16], and will be the subject of further study).

CONCLUSIONS

This study has proposed that the solubility parameter concept model for determining solute retention in reversed-phase liquid chromatographic systems may be recast and examined for its ability to calculate quantitatively the alterations in solute capacity factor for any one system with a change in the eluent composition of that system (eqn. 4). Subsequently, it has been shown that use of Hildebrand's solubility term for predicting both solute behaviour in reversed-phase HPLC and solute aqueous solubility leads to an inherent parameter overestimation by a factor of between 4.2 and 5.0.

Further, for reversed-phase HPLC with aqueous methanol eluents, using derivative equations of the solubility parameter concept model, we have shown how a general semi-empirical relationship between $\log k'_i$ and $\log k'_{w,i}$ may be obtained, which can be used to estimate $\log k'_i$ values at one $\varphi_m$ composition from values at another eluent composition. Additionally, the excellent agreements found between experimentally obtained $\log K_d^{oct}$ values and those estimated using single isocratic $\log k'_i$ values in this general relationship indicates that this distribution coefficient term (which is available for many organic solutes[23], or which may be calculated *a priori*[23]) could be used with eqn. 24 to calculate directly solute retention in ODS–aqueous methanol systems at $\varphi_m = 0.30$–0.75.

SYMBOLS

| | |
|---|---|
| $\gamma$ | activity coefficient at infinite dilution |
| $\delta$ | Hildebrand solubility parameter, $(cal^{1/2} \cdot ml^{-3/2})$; |
| $\varphi$ | volume fraction |
| $\bar{V}$ | molar volume, $(ml \cdot mol^{-1})$ |
| $k'$ | chromatographic capacity factor |
| $n_s/n_m$ | number of moles of stationary phase per mole of mobile phase |
| $X$ | molar fraction aqueous solubility |
| $R$ | gas constant $(cal \cdot mol^{-1} \cdot {}^\circ K^{-1})$ |
| $T$ | absolute temperature $({}^\circ K)$ |
| $K_d^{oct}$ | octan-1-ol–water liquid–liquid distribution coefficient |

*Subscripts*

| | |
|---|---|
| $i$ | solute |
| $j$ | solvent |
| $s$ | stationary phase |
| $m$ | mobile phase |
| $w$ | pure water |
| exp | experimental |
| calc | calculated |

*Superscript*

| | |
|---|---|
| sat | saturated |

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